RECEIVED
CENTRAL FAX CENTER
NOV 2 2 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of Pnina Fishman
Serial No. 09/700,751 Group Art Unit: 1623
Filed: January 4, 2001 Examiner: J. Young
For: PHARMACEUTICAL COMPOSITIONS COMPRISING AN ADENOSINE..

DECLARATION
under Rule 132

Commissioner of Patents and Trademarks
Washington, D.C. 20231

I, Ad P. IJzerman, a Dutch citizen residing at Park Oosterspaarn 6, 2036MB Haarlem, The Netherlands, hereby declare:

1. I am Professor at the Leiden/Amsterdam Center for Drug Research at Leiden University in Leiden, The Netherlands. I am a medicinal chemist with expertise in the field of adenosine receptors.

2. My Curriculum Vitae and list of publications is attached herewith as Annex "A".

3. I have reviewed the patent application in re, serial number 09/700,751 which relates to the use of A_3 adenosine receptor agonists, among other for treating cancer.

4. I am familiar with the manuscript of Mittelman, A. et al (1975) Annals N.Y. Acad. Sci. 225:225-234 (hereinafter "Mittelman"), which relates, among others, to the compound N^6-(Δ^2 isopentenyl)adenosine (hereinafter "IPA").

5. IPA, a bodily substance, is an N^6-substituted adenosine derivative. The corresponding adenine derivative (without the ribose) is a plant cytokinin.

PAGE 33/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

From a literature search I conducted (for manuscripts considered see "Annex B") it appears that IPA has been shown to be active on certain tumor cell lines, with quite a few references to the L-1210 leukemia cell line. None of the manuscripts I considered refer to adenosine receptors to explain the compound's mechanism of action. In fact, it was believed that IPA interferes with methionine metabolism.

6. In conclusion, to me the use of an A_3 adenosine receptor agonist in treating cancer is new and not anticipated by the abovementioned *Mittelman* manuscript. This is corroborated by the fact that the first mentioning of an adenosine A_3 receptor was only in the early nineties (Meyerhof et al, FEBS Lett. 1991;284:155-160; Zhou et al, Proc Natl Acad Sci U S A 1992;89:7432-7436; these references are attached as Annexes "C" and "D", respectively).

7. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: June 29, 2004

Dr. Adi Ijzerman

PAGE 34/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Annex A

CURRICULUM VITAE DR. A. P. IJZERMAN

Name: Adriaan Pieter IJzerman
Date of Birth: 23 December 1954
Place of Birth: Heemstede, The Netherlands

Education

1975 Bachelor's degree in pharmaceutical sciences (Utrecht University)

1979 Master's degree in pharmaceutical sciences (specialisation medicinal chemistry, Utrecht University)

1980 Qualification as a pharmacist (Utrecht University)

1985 Ph.D. degree in medicinal chemistry (Free University of Amsterdam, promoter Prof. dr. H. Timmerman)

Present Employment

Professor of medicinal chemistry at Leiden University, Leiden/Amsterdam Center for Drug Research, division of medicinal chemistry (area: receptor research/molecular modelling; website: www.medchem.leidenuniv.nl). He supervises a reseach group currently consisting of 2 assistant professors, 2 post-doctoral fellows, 5 Ph.D. students, and 3 technicians. He also served as a professor of receptor medicinal chemistry at the Vrije Universiteit in Amsterdam (1998-2002).

He has acted as a copromoter to the following theses.

A. Garritsen, Molecular pharmacology of the adenosine A_1 receptor, 1990
P.J.M. van Galen, Adenosine receptors: structural requirements for agonists and antagonists, 1990
A. van der Bent, Cholecystokinin A receptor antagonists - a medicinal chemistry approach, 1993
A.M. van Rhee, P_2-purinergic receptors - a quest for selective and competitive antagonists, 1993
E.M. van der Wenden, Structural requirements for the interaction between ligands and the adenosine A_1 receptor, 1994
M.W. Beukers, Extracellular breakdown of ATP by human blood cells, 1995
R.A.A. Mathôt, Preclinical pharmacokinetic-pharmacodynamic modelling of the cardiovascular effects of adenosine receptor ligands, 1995

PAGE 35/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

B. van Steen, Structure-affinity relationship studies on 5-HT_{1A} receptor ligands, 1996
W. Kuipers, Receptor-ligand interactions of G protein-coupled receptors - the 5-HT_{1A} receptor as a model, 1996
E.A. van Schaick, Selectivity of adenosine receptor agonists *in vivo*, 1997

As a promoter he has been involved with the following theses.

K. Ingkaninan, Novel procedures for lead finding in plant extracts, 2000
M. de Zwart, Ligands for the human adenosine A_{2B} receptor, 2000
Z-G Gao, Allosteric modulation of G protein-coupled receptors, 2000
E. van Tilburg, Novel partial agonists for adenosine receptors, 2001
J.E. van Muijlwijk-Koezen, Antagonists for the human adenosine A_3 receptor, 2001
M. Schrier, Adenosine and apoptosis in neuroblastoma cells, 2002
A.F. de Ligt, Adenosine A_1 receptors: Constitutive activity, inverse agonism and allosteric modulation, 2003
T.J.H. Bueters, Treatment of organophosphate poisoning with adenosine A_1 receptor agonists, 2003
M.P. Schaddelee, Adenosine A_1 receptor agonists. Blood-brain barrier transport and PK/PD correlations in neuropathic pain, 2003

Research Experience

1980–1985
Ph.D. research and thesis, entitled "The beta-adrenoceptor complex. Requirements for the interaction with its ligands."

1985-today
within the division of medicinal chemistry research is focussed on purinergic (adenosine) receptors and nucleoside transport proteins. These proteins are tools in the broader perspective of the main theme of research, *viz.* the understanding of the mechanisms of interaction between a small molecule (i.e., a drug, a hormone, a neurotransmitter) and receptor proteins.

Awards

1979 research award Utrecht University

1987 Millipore Science Education Award

PAGE 36/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

1997 Rottendorf-Europa-Preis

2000 Science Teaching Award (Leiden University)

2001 "Tulip-and-Oak" medal, presented at the 13th Noordwijkerhout-Camerino Symposium

2001 Nomination Leiden University Best Teacher

2003 Nomination Leiden University Best Teacher

Publications

Dr. IJzerman is the (co)author of approx. 150 publications in international scientific journals. He lectured upon invitation at numerous conferences.

Further Scientific Activities

- Member of the board of the medicinal chemistry division of the Royal Dutch Chemical Society (1989 - 1995)
- Member of the board of the Dutch Pharmacological Society (1997-2001)
- Member of the Scientific Chapter to the New Drug Research Foundation (1997-1999)
- Member of STIGON (promotion of start-up pharmaceutical business initiatives) (1999-2003)
- Chairman of FIGON (Dutch Federation for Innovative Drug Research) (2000-2004)
- Member of the IUPHAR adenosine receptor nomenclature committee (1997-today)
- Referee to
  Molecular Pharmacology
  Journal of Medicinal Chemistry
  Biochemical Pharmacology
  European Journal of Medicinal Chemistry
  European Journal of Pharmacology
  European Journal of Pharmaceutical Sciences
  Drug Design and Discovery
  Drug Development Research
  Pharmaceutical Research
  General Pharmacology
  Neurochemistry International
  Life Sciences
  Nucleosides & Nucleotides
  Journal of Neurochemistry
  Journal of Pharmacology and Experimental Therapeutics
  Journal of Receptor Research & Signal Transduction
  Receuil des Travaux Chimiques des Pays-Bas
  Environmental Toxicology and Pharmacology
  PROTEINS: Structure, Function, and Genetics

PAGE 37/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Journal of Ethnopharmacology
Journal of Chemical Crystallography
British Journal of Pharmacology
Neuropharmacology
Bioorganic & Medicinal Chemistry
Bioorganic & Medicinal Chemistry Letters
Trend in Pharmacological Sciences
Journal of Controlled Release
Genomes
Brain Research
FEBS Letters
Tetrahedron

- Chairman of the organisation committee and member of the scientific committee of the international symposium "Pharmacology of purinergic receptors. Implications for drug design" (Noordwijk, 6 - 8 July 1990)
- Member of the organisation committee of the 6th International Conference on Retinal Proteins (Leiden, 19 - 24 June 1994)
- Organiser of LACDR 'School on medicinal chemistry', Noordwijkerhout, October 27 - 30, 1992; October 26 - 29, 1993; October 25 - 28, 1994; October 24 - 27, 1995, October 22 - 25, 1996; October 27 - 30, 1997; October 27-30, 1998; October 26-29, 1999; October 24-27, 2000; October 23-26, 2001; October 22-25, 2002; October 28-31, 2003.
- Chairman of the organisation and scientific committee of the international workshop on Inverse Agonism, Barcelona, June 22-24, 2000
- Chairman of the organisation committee of the Esteve symposium on Inverse Agonism, Hostal de S'Agaro, October 2-5, 2002
- Member of the scientific and organisation committees of several congresses and symposia organised by various Dutch bodies
- Member of several election committees for full professorships in the Netherlands
- Scientific advisor at the NIH/NIDDK, Bethesda, USA (May/June 1991)
- Participant in several courses on 'research management' and 'human resource management'
- Member of the editorial board of Drug Development Research (1992-today)
- Member of the editorial board of Drug Design and Discovery (1992-1997)
- Member of the editorial board of Molecules (an electronic journal) (1999-today)
- Member of the editorial board of Drug Design and Reviews - Online (2003-today)
- Programme Coordinator of granted EC BIOMED concerted action 'Adenosine receptors in the brain (ADEURO)' (1994-1996)

PAGE 38/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

- Managing co-director of granted EC BIOTECH programme 'Molecular mechanisms of beta-adrenergic receptor function and regulation (EUROCEPTOR)' (1993-1996)
- Managing co-director in granted EC BIOTECH programme 'An advanced data management system for G protein-coupled receptors (GPCRDB)' (1996-1999)
- Programme coordinator of granted EC BIOMED programme 'Inverse agonism. Implications for drug design' (1997-2000)

PAGE 39/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Publications of Dr. IJzerman

Wilting J, Kremer JMH, IJzerman AP, Schulman SG.
The kinetics of the binding of warfarin to human serum albumin as studied by stopped-flow spectrophotometry.
Biochim. Biophys. Acta 706, 96 - 104 (1982).

IJzerman AP, Bultsma T, Timmerman H, Zaagsma J.
The ionization of beta-adrenoceptor ligands: a method for unravelling ionization schemes.
J. Pharm. Pharmacol. 36, 11 - 15 (1984).

IJzerman AP, Bultsma T, Timmerman H, Zaagsma J.
The relation between ionization and affinity of beta-adrenoceptor ligands.
Naunyn-Schmiedeberg's Arch. Pharmacol. 327, 293 - 298 (1984).

IJzerman AP, Dorlas R, Aué GHJ, Timmerman H.
Factors controlling $beta_1$-adrenoceptor affinity and selectivity.
Biochem. Pharmacol. 34, 2883 - 2890 (1985).

IJzerman AP, Aué GHJ, Bultsma T, Linschoten MR, Timmerman H.
Quantitative evaluation of the $beta_2$-adrenoceptor affinity of phenoxypropanolamines and phenylethanolamines.
J. Med. Chem. 28, 1328 - 1334 (1985).

IJzerman AP.
The beta-adrenoceptor complex. Requirements for the interaction with its ligands (Ph. D. thesis).
Elinkwijk BV, Utrecht, 1985.

Linschoten MR, Bultsma T, IJzerman AP, Timmerman H.
Mapping the turkey erythrocyte beta-receptor: a distance geometry approach.
J. Med. Chem. 29, 278 - 286 (1986).

IJzerman AP, Bultsma T, Timmerman H.
Quantitative evaluation of the $beta_2$-adrenoceptor intrinsic activity of N-tert.butyl phenylethanolamines.
J. Med. Chem. 29, 549 - 554 (1986).

IJzerman AP, Bultsma T, Timmerman H.
Binding characteristics of the regulatory guanine nucleotide binding protein, and the activation of the enzyme adenylate cyclase, present in a bovine skeletal muscle membrane preparation.
Res. Comm. Chem. Pathol. Pharmacol. 52, 93 - 105 (1986).

IJzerman AP.
The beta-adrenoceptor complex (abstract of Ph. D. thesis).
Pharmaceut. Weekbl. Sci. Ed. 8, 155 - 157 (1986).

PAGE 40/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

IJzerman AP, Timmerman H.
The beta-adrenoceptor/adenylate cyclase complex. From model to biochemical reality (review).
Pharmaceut. Weekbl. Sci. Ed. 8, 209 - 222 (1986).

Severne Y, IJzerman AP, Nerme V, Timmerman H, Vauquelin G.
Shallow agonist competition binding curves for beta-adrenergic receptors: the role of tight agonist binding.
Mol. Pharmacol. 31, 69 - 73 (1987).

Galen PJM v, IJzerman AP, Soudijn W.
Adenosine derivatives with N^6-alkyl, -alkylamine or -alkyladenosine substituents as probes for the A_1-receptor.
FEBS Lett. 223, 197 -201 (1987).

IJzerman AP, Nagesser A, Garritsen A.
The membrane stabilizing activity of ß-adrenoceptor ligands.
Biochem. Pharmacol. 36, 4239 - 4244 (1987).

Garritsen A, IJzerman AP, Soudijn W.
[^{3}H]Batrachotoxinin-A 20-α-benzoate binding to sodium channels in rat brain: sensitivity to tetrodotoxin and divalent cations.
Eur. J. Pharmacol. 145, 261 - 266 (1988)

IJzerman AP.
Receptor models and mechanisms. Perspectives for new drugs.
Pharmaceut. Weekbl. 123, 378 - 382 (1988)

Debing I, IJzerman AP, Vauquelin G. Melanosome binding and oxidation - reduction properties of synthetic l-DOPA-melanine as in vitro tests for drug toxicity.
Mol. Pharmacol. 33, 470 - 476 (1988)

IJzerman AP, Vlijmen HWT v.
A molecular graphics study exploring a putative ligand binding site of the ß-adrenoceptor.
J. Comp. Aid. Molec. Des. 2, 43 - 53 (1988)

IJzerman AP.
Ionization constants of sparingly soluble substances from aqueous titration data.
Int. J. Pharmaceut. 46, 173 - 175 (1988)

IJzerman AP.
Limiting solubilities and ionization constants of sparingly soluble compounds: determination from aqueous potentiometric titration data only.
Pharmaceut. Res. 5, 772 - 775 (1988)

IJzerman AP, Soudijn W.
The antiarrhythmic action of beta-adrenoceptor antagonists (review).
TiPS 10, 31 - 36 (1989)

PAGE 41/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Galen PJM v, Leusen FJJ, IJzerman AP, Soudijn W.
Mapping the N^6-region of the adenosine-A_1 receptor using computer graphics.
Eur. J. Pharmacol. 172, 19 - 27 (1989)

Garritsen A, IJzerman AP, Soudijn W.
Adenosine A_1 receptors are not coupled to Ca^{2+} uptake in rat brain synaptosomes. Biochem. Pharmacol. 38, 693 - 695 (1989)

IJzerman AP, Menkveld GJ, Thedinga KH.
A refined method for the photoaffinity labelling of the nucleoside transport protein: application to cell membranes of calf lung tissue. Biochim. Biophys. Acta 979, 153 - 156 (1989)

Pirovano IM, IJzerman AP, Galen PJM v, Soudijn W.
The influence of molecular structure of N^6-(w-aminoalkyl)-adenosines on adenosine receptor affinity and intrinsic activity.
Eur. J. Pharmacol. 172, 185 - 193 (1989)

Vlijmen HWT v, IJzerman AP.
Molecular modeling of a probable ligand binding site on the ß-adrenergic receptor.
J. Comp. Aid. Molec. Des. 3, 165 - 174 (1989)

IJzerman AP, Thedinga KH, Custers AFCM, Hoos B, Van Belle H.
Inhibition of nucleoside transport by a new series of compounds related to lidoflazine and mioflazine. Eur. J. Pharmacol. 172, 273 - 281 (1989)

Galen PJM v, IJzerman AP, Soudijn W.
Xanthine-7-ribosides as adenosine A_1 receptor antagonists: further evidence for adenosine's anti mode of binding.
Nucleosides & Nucleotides 9, 275 - 291 (1990)

Galen PJM v, Vlijmen HWT v, IJzerman AP, Soudijn W.
A model for the antagonist binding site on the adenosine A_1 receptor based on steric, electrostatic and hydrophobic properties.
J. Med. Chem. 33, 1708 - 1713 (1990)

Garritsen A, IJzerman AP, Beukers MW, Cragoe EJ Jr, Soudijn W.
Interaction of amiloride and its analogues with adenosine A_1 receptors in calf brain.
Biochem. Pharmacol. 40, 827 - 834 (1990)

Garritsen A, IJzerman AP, Beukers MW, Soudijn W.
Chemical modification of adenosine A_1 receptors: implications for the interaction with PIA, DPCPX and amiloride.
Biochem. Pharmacol. 40, 835 - 842 (1990)

IJzerman AP, Voorschuur AH.
The relationship between ionization and affinity of nucleoside transport inhibitors.
Naunyn-Schmiedeberg's Arch. Pharmacol. 342, 336 - 341 (1990)

PAGE 42/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

IJzerman AP, Galen PJM v.
Pharmacology of purinergic receptors: implications for drug design.
TIPS 11, 342 - 343 (1990)

Pirovano IM, Van Belle H, IJzerman AP.
Inhibition of nucleoside uptake in human erythrocytes by a new series of compounds related to lidoflazine and mioflazine.
Eur. J. Pharmacol. - Mol. Pharmacol. Sect. 189, 419 - 422 (1990)

Galen PJM v, Nissen P, Wijngaarden I v, IJzerman AP, Soudijn W.
1*H*-Imidazo[4,5-c]quinolin-4-amines: novel non-xanthine adenosine antagonists.
J. Med. Chem. 34, 1202 - 1206 (1991)

Garritsen A, IJzerman AP, Tulp MTM, Cragoe Jr. EJ, Soudijn W.
Receptor binding profiles of amiloride analogues provide no evidence for a link between receptors and the Na^+/H^+ exchanger, but indicate a common structure on receptor proteins.
J. Receptor Res. 11, 891 - 907 (1991)

Garritsen A, Beukers MW, IJzerman AP, Soudijn W.
Recognition of adenosine receptors by amiloride and its analogues.
Nucleosides & Nucleotides 10, 1107 - 1111 (1991)

IJzerman AP, Galen PJM v, Vlijmen HWT v, Soudijn W, Nissen P, Wijngaarden I v.
Molecular modelling of the antagonist binding site on the adenosine A_1 receptor.
Nucleosides & Nucleotides 10, 1039 - 1047 (1991)

Wenden EM vd, Galen PJM v, IJzerman AP, Soudijn W.
A model for the hydrogen bonding interactions between adenosine receptor ligands and histidyl residues in the adenosine A_1 receptor binding site, based on AM1 calculations.
J. Mol. Struct. (Theochem) 231, 175 - 184 (1991)

Wenden EM vd, Galen PJM v, IJzerman AP, Soudijn W.
Mapping the C8-region of the adenosine A_1 receptor with computer graphics.
Eur. J. Pharmacol. - Mol. Pharmacol. Sect. 206, 315 - 323 (1991)

Hoogstrate AJ, Verhoef J, Brussee J, IJzerman AP, Spies F, Bodde H.
Kinetics, ultrastructural aspects and molecular modelling of transdermal peptide flux enhancement by N-alkylazacycloheptanones.
Int. J. Pharmaceutics 76, 37 - 47 (1991)

PAGE 43/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Garritsen A, Beukers MW, IJzerman AP, Cragoe Jr. EJ, Soudijn W.
The mode of interaction of amiloride and its analogues with the adenosine A_1 receptor.
Neurochem. Int. 20, 207 -213 (1992)

IJzerman AP, Melman CTM.
Chemical modification of cholecystokinin-A receptors in rat pancreatic membranes.
Eur. J. Biochem. 203, 521 - 526 (1992)

IJzerman AP, Kruidering M, Van Weert A, Van Belle H, Janssen C.
[^{3}H]R75231 - a new radioligand for the nitrobenzylthioinosine sensitive nucleoside transport proteins.
Naunyn-Schmiedeberg's Arch. Pharmacol. 345, 558 - 563 (1992)

Van der Wenden EM, IJzerman AP, Soudijn W.
A steric and electrostatic comparison of three models for the agonist/antagonist binding site on the adenosine A_1 receptor.
J. Med. Chem. 35, 629 - 635 (1992)

Van der Bent A, ter Laak AM, IJzerman AP, Soudijn W.
Molecular modelling of asperlicin derived cholecystokinin A receptor antagonists.
Eur. J. Pharmacol. - Mol. Pharmacol. Sect. 226, 327 - 334 (1992)

Van der Bent A, Blommaert AGS, Melman CTM, IJzerman AP, van Wijngaarden I, Soudijn W.
Hybrid cholecystokinin-A antagonists based on molecular modeling of lorglumide and L-364,817.
J. Med. Chem. 35, 1042 - 1049 (1992)

IJzerman AP, Van Galen PJM, Jacobson KA.
Molecular modeling of adenosine receptors. I. The ligand binding site on the A_1 receptor.
Drug Design and Discovery 9, 49 - 67 (1992)

Van Galen PJM, Melman N, IJzerman AP, Jacobson KA.
Characterization of [^{35}S]ADPbetaS binding to bovine brain membranes.
Pharmacol. Commun. 1, 279 - 290 (1992)

IJzerman AP.
Structural analysis of kappa-opioid receptor agonists
Recl. Trav. Chim. Pays-Bas 112, 169 - 173 (1993)

Van Rhee AM, Van Winden ECA, Nagelkerke JF, De Bont HJGM, IJzerman AP, Soudijn W.
Binding of the radioligand [^{35}S]adenosine-5'-O-(2-thiodiphosphate) and intracellular calcium response in rat liver parenchymal cells.
Biochemical Pharmacology 45, 801 - 807 (1993)

PAGE 44/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Dudley MW, Peet NP, Demeter DA, Weintraub HJR, IJzerman AP, Nordvall G, Van Galen PJM, Jacobson KA.
Adenosine A_1 receptor and ligand molecular modeling.
Drug Dev. Res. 28, 237 - 243 (1993)

Mathôt RAA, Appel S, Van Schaick EA, Soudijn W, IJzerman AP, Danhof M.
High-performance liquid chromatography of the adenosine A_1 agonist N^6-cyclopentyladenosine and the A_1 antagonist 8-cyclopentyltheophylline and its application in a pharmacokinetic study in rats.
J. Chromatography - Biomed. Applic. 620, 113 - 120 (1993)

Beukers MW, Pirovano IM, Van Weert A, Kerkhof CJM, IJzerman AP, Soudijn W.
Characterization of ecto-ATPase on human blood cells. A physiological role in platelet aggregation?
Biochem. Pharmacol. 46, 1959 - 1966 (1993)

Van der Bent A, Van den Brink I, IJzerman AP, Van Wijngaarden I, Soudijn W.
Synthesis and biological evaluation of lorglumide-like hybrid cholecystokinin-A receptor antagonists.
Drug Development Research 31, 197 - 205 (1994)

Beukers MW, Kerkhof CJM, IJzerman AP, Soudijn W.
Nucleoside transport inhibition and platelet aggregation in human blood: R75231 and its enantiomers, draflazine and R88016.
Eur. J. Pharmacol. - Mol. Pharm. Sect. 266, 57 - 62 (1994)

Crack BE, Beukers MW, McKechnie KCW, IJzerman AP, Leff P.
Pharmacological analysis of ecto-ATPase inhibition: evidence for combined enzyme inhibition and receptor antagonism in P_{2x}-purinoceptor ligands.
Br. J. Pharmacol. 113, 1432 - 1438 (1994)

Van Rhee AM, Van der Heijden MPA, Beukers MW, IJzerman AP, Soudijn W.
Novel competitive antagonists for P_2 purinoceptors.
Eur. J. Pharmacol. - Mol. Pharm. Sect. 268, 1 - 7 (1994)

Kuipers W, Van Wijngaarden I, IJzerman AP.
A model of the serotonin 5-HT_{1A} receptor: agonist and antagonist binding sites.
Drug Design & Disc. 11, 231 - 249 (1994)

IJzerman AP, Van der Wenden EM, Van Galen PJM, Jacobson KA.
Molecular modeling of adenosine receptors. II. The ligand binding site on the rat A_{2a} receptor.
Eur. J. Pharmacol. - Mol. Pharm. Sect. 268, 95 - 104 (1994)

PAGE 45/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Borea PA, Varani K, Dalpiaz A, Capuzzo A, Fabbri E, IJzerman AP.
Full and partial agonistic behaviour and thermodynamic binding parameters of adenosine A_1 receptor ligands.
Eur. J. Pharmacol. - Mol. Pharm. Sect. 267, 55 - 61 (1994)

Mathôt RAA, Van den Aarsen BCFM, Von Frijtag Drabbe Künzel JK, Danhof M, IJzerman AP.
Assessment of the enantiomeric purity of R- and S-N^6-phenylisopropyladenosine (PIA): implications for receptor subclassification.
Naunyn-Schmiedeberg's Arch. Pharmacol. 350, 109 - 112 (1994)

Mathôt RAA, Van Schaick EA, Soudijn W, Breimer DD, IJzerman AP, Danhof M.
Pharmacokinetic-pharmacodynamic relationship of the cardiovascular effects of the adenosine A_1 receptor agonist N^6-cyclopentyladenosine (CPA) in the rat.
J. Pharmacol. Exp. Ther. 268, 616 - 624 (1994)

Van Galen PJM, Van Bergen AH, Gallo-Rodriguez C, Melman N, Olah ME, IJzerman AP, Stiles GL, Jacobson KA.
A binding site model and structure-activity relationships for the rat A_3 adenosine receptor.
Mol. Pharmacol. 45, 1101 - 1111 (1994)

Kennedy C, IJzerman AP.
Adenosine and ATP: from receptor structure to clinical applications (meeting report).
TIPS 15, 311-312 (1994)

Irth H, Cleton A, Mathôt RAA, Danhof M, IJzerman AP, Tjaden UR, Van der Greef J.
Liquid chromatographic determination of the adenosine receptor agonist CGS 21680 in blood using on-line solid-phase extraction on a phenylboronic acid support and fluorescence detection.
J. Chromat. B 658, 207 - 212 (1994)

Van der Bent A, IJzerman AP, Soudijn W.
Molecular modelling of CCK-A receptors.
Drug Design & Discovery 12, 129 - 148 (1994)

IJzerman AP, Van der Wenden EM, Von Frijtag Drabbe Künzel JK, Mathôt RAA, Danhof M, Borea PA, Varani K.
Partial agonism of theophylline-7-riboside on adenosine receptors.
Naunyn-Schmiedeberg's Arch. Pharmacol. 350, 638 - 645 (1994)

Ceulemans G, Busson R, Weyns N, Vandendriessche F, Rozenski J, IJzerman AP, Herdewijn P.
Synthesis of 3'-fluoro-3'-deoxy-N^6-cyclopentyladenosine.
Nucleosides & Nucleotides 13, 1991 - 2000 (1994)

PAGE 46/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

IJzerman AP, Von Frijtag Drabbe Künzel JK, Vittori S, Cristalli G.
Purine-substituted adenosine derivatives with small N^6-substituents as adenosine receptor agonists.
Nucleosides & Nucleotides 13, 2267 - 2281 (1994)

IJzerman AP, Van Galen PJM, Van der Wenden EM.
Molecular modelling of the adenosine A_1 receptor.
In: New Perspectives in Drug Design (Newton CG et al, eds.), Academic Press (London), 1995, pp. 119 - 136

IJzerman AP, Van der Wenden EM, Van Galen PJM, Jacobson KA.
Molecular modeling of adenosine A_1 and A_{2a} receptors.
In: Adenosine and adenine nucleotides: from molecular biology to integrative physiology (Belardinelli L and Pelleg A, eds), Kluwer (Norwell MA, USA), 1995, pp. 27 - 37

Crack BE, Pollard CE, Beukers MW, Roberts SM, Hunt F, Ingall AH, McKechnie KCW, IJzerman AP, Leff P.
Pharmacological and biochemical analysis of FPL67156, a novel, selective inhibitor of ecto-ATPase.
Br. J. Pharmacol. 114, 475 - 481 (1995)

Twisk J, Hoekman MFM, Muller LM, Tamaru T, IJzerman A, Mager WH, Princen HMG.
Structural aspects of bile acids involved in regulation of cholesterol 7α-hydroxylase and sterol 27-hydroxylase.
Eur. J. Biochem. 228, 596 - 604 (1995)

Mathôt RAA, Cleton A, Soudijn W, IJzerman AP, Danhof M.
Pharmacokinetic modelling of the haemodynamic effects of the A_{2a} adenosine receptor agonist CGS 21680C in conscious, normotensive rats.
Br. J. Pharmacol. 114, 761 - 768 (1995)

Mathôt RAA, Van den Aarsen BCFM, Soudijn W, Breimer DD, IJzerman AP, Danhof M.
Pharmacokinetic-pharmacodynamic modelling of the cardiovascular effects of R- and S-N^6-phenylisopropyladenosine (PIA) in conscious, normotensive rats.
J. Pharm. Exp. Ther. 273, 405 - 414 (1995)

Beukers MW, Kerkhof CJM, Van Rhee MA, Ardanuy U, Gurgel C, Widjaja H, Nickel P, IJzerman AP, Soudijn W.
Suramin analogs, divalent cations and ATP$_7$S as inhibitors of ecto-ATPase.
Naunyn-Schmiedeberg's Arch. Pharmacol. 351, 523 - 528 (1995)

Van der Wenden EM, Von Frijtag Drabbe Kunzel JK, Mathot RAA, Danhof M, IJzerman AP, Soudijn W.
Ribose-modified adenosine analogues as potential partial agonists for the adenosine receptor.
J. Med. Chem. 38, 4000 - 4006 (1995)

PAGE 47/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Van der Wenden EM, Hartog-Witte HR, Roelen H, Von Frijtag Drabbe Kunzel JK, Pirovano IM, Mathot RAA, Danhof M, Van Aerschot A, Lidaks MJ, IJzerman AP, Soudijn W.
8-Substituted adenosine and theophylline-7-riboside analogues as potential partial agonists for the adenosine A_1 receptor.
Eur. J. Pharmacol. - Mol. Pharm. Sect. 290, 189 - 199 (1995)

Appel S, Mathôt RAA, Langemeijer MWE, IJzerman AP, Danhof M.
Modelling of the *in vivo* pharmacodynamic interaction of an A_1 adenosine receptor agonist and antagonist: N^6-cyclopentyladenosine and 8-cyclopentyltheophylline.
Br. J. Pharmacol. 115, 1253 - 1259 (1995)

Siddiqi SM, Esker JL, Olah ME, Ji X, Melman N, Tiwari KN, Secrist III JA, Cristalli G, Stiles GL, Johnson CR, IJzerman AP, Jacobson KA.
Search for new leads for ligand selectivity at adenosine receptors.
J. Med. Chem. 38, 1174 - 1188 (1995)

Mathôt RAA, Van der Wenden EM, Soudijn W, IJzerman AP, Danhof M.
Deoxyribose analogues of N^6-cyclopentyladenosine (CPA) are partial agonists at the adenosine A_1 receptor in vivo.
Br. J. Pharmacol. 116, 1957 - 1964 (1995)

Mathôt RAA, Gubbens-Stibbe JM, Soudijn W, Jacobson KA, IJzerman AP, Danhof M.
Quantification of the in vivo potency of the adenosine A_2 receptor antagonist 8-(3-chlorostyryl)caffeine (CSC).
J. Pharmacol. Exp. Ther. 275, 245 - 253 (1995)

Van der Wenden EM, Price SL, Apaya RP, IJzerman AP, Soudijn W.
Relative binding orientations of adenosine A_1 receptor ligands - a test case for Distributed Multipole Analysis in medicinal chemistry.
J. Comput.-Aided Mol. Design 9, 44 - 54 (1995)
(also on the Internet:
http://wucmd.wustl.edu/jcamd/281/paper.html)

Kuipers W, Van Wijngaarden I, Kruse CG, Ter Horst - Van Amstel M, Tulp MTM, IJzerman AP.
N^4-Unsubsituted N^1-arylpiperazines as high-affinity 5-HT_{1A} receptor ligands.
J. Med. Chem. 38, 1942 - 1954 (1995)

Verheggen I, Van Aerschot A, Pillet N, Van der Wenden EM, IJzerman A, Herdewijn P.
Synthesis of 1,5-anhydro-2-(N^6-cyclopentyladenin-9-yl)-2-deoxy-D-*altro*hexitol.
Nucleosides & Nucleotides 14, 321 - 324 (1995)

PAGE 48/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

IJzerman AP, Zuurmond HM.
Molecular modelling of ß-adrenoceptors.
In: Membrane protein models: experiment, theory and speculation (Findlay J, ed), BIOS Scientific Publishers (Oxford), 1996, pp. 133 - 144

Kuipers W, Oliveira L, Paiva ACM, Rippmann F, Sander C, Vriend G, IJzerman AP.
Analysis of G protein-coupled receptor function.
In: Membrane protein models: experiment, theory and speculation (Findlay J, ed), BIOS Scientific Publishers (Oxford), 1996, pp. 27 - 45

IJzerman AP, Van der Wenden EM, Roelen HCPF, Mathôt RAA, Von Frijtag Drabbe Künzel JK.
Partial agonists for adenosine receptors.
In: "Perspectives in Receptor Research", Pharmacochemistry Library Series (Giardinà D, ed.), Elsevier Science Publishers, Amsterdam, 1996, pp. 181 - 192.

IJzerman AP, Von Frijtag Drabbe Künzel JK, Kim J, Jiang Q, Jacobson KA.
Site-directed mutagenesis of the human A_{2A} adenosine receptor. Critical involvement of Glu^{13} in agonist recognition.
Eur. J. Pharmacol. 310, 269 - 272 (1996)

Mathôt RAA, Soudijn W, Breimer DD, IJzerman AP, Danhof M.
Pharmacokinetic-hemodynamic relationships of 2-chloroadenosine: assessment of the potency and intrinsic activity at adenosine A_1 and A_{2a} receptors *in vivo*.
Br. J. Pharmacol. 118, 369 - 377 (1996)

Mathôt RAA, Van der Wenden EM, Soudijn W, Breimer DD, IJzerman AP, Danhof M.
Partial agonism of the non-selective adenosine receptor agonist 8-butylaminoadenosine at the A1 receptor in vivo.
J. Pharmacol. Exp. Ther. 279, 1439-1446 (1996)

Von Frijtag Drabbe Künzel JK, Van der Zee J, IJzerman AP.
Radical scavenging properties of adenosine and derivatives *in vitro*.
Drug Dev. Res. 37, 48 - 54 (1996)

Barbhaiya H, McClain R, IJzerman AP, Rivkees SA.
Site-directed mutagenesis of the human A_1 adenosine receptor: influences of acidic amino acids on agonist binding.
Mol. Pharmacol. 50, 1635 - 1642 (1996)

Roelen H, Veldman N, Spek AL, Von Frijtag Drabbe Kunzel JK, Mathot RAA, IJzerman AP.
N^6,C8-disubstituted adenosine derivatives as partial agonists for adenosine A_1 receptors.
J. Med. Chem. 39, 1463 - 1471 (1996)

PAGE 49/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Beindl W, Mitterauer T, Hohenegger M, IJzerman AP, Nanoff C, Freissmuth M.
Inhibition of receptor/G protein coupling by suramin analogues.
Mol. Pharmacol. 50, 415 - 423 (1996)

Freissmuth M, Boihm S, Beindl W, Nickel P, IJzerman AP, Hohenegger M, Nanoff C.
Suramin analogs as subtype-selective G protein inhibitors.
Mol. Pharmacol. 49, 602 - 611 (1996)

Wieland K, Zuurmond HM, Krasel C, IJzerman AP, Lohse MJ.
Involvement of Asn-293 in stereospecific agonist recognition and in activation of the ß$_2$-adrenergic receptor.
Proc. Natl. Acad. Sci. USA 93, 9276 - 9281 (1996)

Van Schaick EA, Jacobson KA, Kim HO, IJzerman AP, Danhof M.
Hemodynamic effects and histamine release elicited by the selective adenosine A_3 receptor agonist 2-Cl-IB-MECA in conscious rats.
Eur. J. Pharmacol. 308, 311 - 314 (1996)

Van Schaick EA, De Greef HJMM, Langemeijer MWE, Sheehan MJ, IJzerman AP, Danhof M.
Pharmacokinetic-pharmacodynamic modelling of the anti-lipolytic and anti-ketotic effects of the adenosine A_1-receptor agonist N^6-(p-sulfophenyl)adenosine in rats.
Br. J. Pharmacol. 122, 525 - 533 (1997)

IJzerman AP, Van der Wenden EM.
Modulators of adenosine uptake, release and inactivation.
In "Purinergic approaches in experimental therapeutics" (Jacobson KA and Jarvis M, eds), John Wiley & Sons, New York, 1997, pp. 129 - 148

Van Schaick EA, Kulkarni C, Von Frijtag Drabbe Künzel JK, Mathôt RAA, Cristalli G, IJzerman AP, Danhof M.
Kinetics of action of three adenosine A_1 receptor agonists with differing lipophilicity in rats: comparison of pharmacokinetic, henodynamic and EEG effects.
Naunyn-Schmiedeberg's Arch. Pharmacol. 356, 827 - 837 (1997)

Kuipers W, Oliveira L, Vriend G, IJzerman AP.
Identification of class-determining residues in G protein-coupled receptors by sequence analysis.
Receptors & Channels 5, 159 - 174 (1997)

Van Schaick EA, De Greef HJMM, IJzerman AP, Danhof M.
Physiological indirect effect modelling of the anti-lipolytic effects of adenosine A_1 receptor agonists.
J. Pharmacokin. Biopharm. 25, 673 - 694 (1997)

PAGE 50/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Kuipers W, Link R, Standaar PJ, Stoit AR, Van Wijngaarden I, Leurs R, IJzerman AP.
Study of the interaction between aryloxypropanolamines and Asn386 in helix VII of the human 5-HT_{1A} receptor.
Mol. Pharmacol. 51, 889 - 896 (1997)

Kuipers W, Kruse CG, Van Wijngaarden I, Standaar PJ, Tulp MTM, Veldman N, Spek AL, IJzerman AP.
5-HT_{1A}- versus D_2-receptor selectivity of flesinoxan and analogous N^4-substituted N^1-arylpiperazines.
J. Med. Chem. 40, 300 - 312 (1997)

Smeets RLL, IJzerman AP, Hermsen HPH, Ophorst OJAE, Van Emst-de Vries SE, DePont JJHHM, Willems PHGM.
Functional characterization by site-directed mutagenesis of the putative devazepide binding site of the cholecystokinin-A receptor.
Eur. J. Pharmacol. 325, 93 - 99 (1997)

Bol CJJG, IJzerman AP, Danhof M, Mandema JW.
Determination of dexmedetomidine in rat plasma by a sensitive [^{3}H]clonidine radioreceptor assay.
J. Pharmaceut. Sci. 86, 822 - 826 (1997)

Lorenzen A, Sebastiao AM, Sellink A, Vogt H, Schwabe U, Ribeiro JA, IJzerman AP.
Biological activities of N^6,C8-disubstituted adenosine derivatives as partial agonists at rat brain adenosine A_1 receptors.
Eur. J. Pharmacol. 334, 299 - 307 (1997)

Van der Graaf PH, Van Schaick EA, Mathot RAA, IJzerman AP, Danhof M.
Mechanism-based pharmacokinetic-pharmacodynamic modeling of the effects of N^6-cyclopentyladenosine analogs on heart rate in rat: estimation of *in vivo* operational affinity and efficacy at adenosine A_1 receptors.
J. Pharmacol. Exp. Ther. 283, 809 - 816 (1997)

Van Calenbergh S, Von Frijtag Drabbe Künzel JK, Blaton NM, Peeters OM, Rozenski J, Van Aerschot A, De Bruyn A, De Keukeleire D, IJzerman AP, Herdewijn P.
N^6-Cyclopentyl 3'-substituted xylofuranosyl adenosines: a new class of non-xanthine adenosine A_1 receptor antagonists.
J. Med. Chem. 40, 3765 - 3772 (1997)

Van Calenbergh S, IJzerman AP, Herdewijn P.
Compounds derived from adenosine, use of such compound as a medicament, method for synthesizing such a compound and intermediates thereof.
EP 97.200622.5, issued March 3, 1997

Van Schaick EA, Mathôt RAA, Gubbens-Stibbe JM, Langemeijer MWE, IJzerman AP, Danhof M.

PAGE 51/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

8-Alkylamino substiuted analogues of N^6-cyclopentylaminoadenosine (CPA) are partial agonists for the cardiovascular adenosine A_1-receptors *in vivo*.
J. Pharmacol. Exp. Ther. 283, 800 - 808 (1997)

De Zwart M, Link R, Von Frijtag Drabbe Künzel JK, Cristalli G, Jacobson KA, Townsend-Nicholson A, IJzerman AP.
A screening of adenosine analogues on the human adenosine A_{2B} receptor as part of a search for potent and selective agonists.
Nucleosides & Nucleotides 17, 969 - 986 (1998)

Bouwstra JA, Gooris GS, Dubbelaar FER, Weerheim AM, IJzerman AP, Ponec M.
The role of ceramide 1 in the molecular organization of the striatum corneum lipids.
J. Lipid Res. 39, 186 - 196 (1998)

IJzerman AP, Van der Wenden EM, Kuipers W.
Computational chemistry in receptor-based drug design.
In: Receptor-based drug design (P. Leff, ed), Marcel Dekker Inc, New York, 1998, pp 323 - 344.

Van Schaick EA, Tukker HE, Roelen HCPF, IJzerman AP, Danhof M.
Selectivity of action of 8-alkylamino analogues of N^6-cyclopentyladenosine *in vivo*: hemodynamic versus anti-lipolytic responses in rats.
Br. J. Pharmacol. 124, 607 - 618 (1998)

Kim YC, De Zwart M, Chang L, Moro S, von Frijtag Drabbe Künzel JK, Melman N, IJzerman AP, Jacobson KA.
Derivatives of the triazoloquinazoline adenosine antagonist (CGS15943) having high potency at the human A_{2B} and A_3 receptor subtypes.
J. Med. Chem. 41, 2835 - 2845 (1998)

Van Calenbergh S, IJzerman AP, Herdewijn P.
3'-Amidated 3'-deoxyxylofuranose analogs of N^6-cyclopentyladenosine - a new class of non-xanthine antagonists at the adenosine A_1 receptor.
Nucleosides & Nucleotides 17, 1571 - 1576 (1998)

Van Schaick EA, Zuideveld KP, Tukker HE, Langemeijer MWE, IJzerman AP, Danhof M.
Metabolic and cardiovascular effects of the adenosine A_1 receptor agonist N^6-(p-sulfophenyl)adenosine in diabetic Zucker rats; influence of the disease on the selectivity of action.
J. Pharmacol. Exp. Ther. 287, 21 - 30 (1998)

Van der Wenden EM, Carnielli M, Roelen HCPF, Lorenzen A, von Frijtag Drabbe Küunzel JK, IJzerman AP.
5'-Substituted adenosine analogs as new high affinity partial agonists for the adenosine A_1 receptor.
J. Med. Chem. 41, 102 - 108 (1998)

PAGE 52/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Van Muijlwijk-Koezen JE, Timmerman H, Link R, Van der Goot H, IJzerman AP.
A novel class of adenosine A_3 receptor ligands. I. 3-(2-Pyridinyl)isoquinoline derivatives.
J. Med. Chem. 41, 3987 - 3993 (1998)

Van Muijlwijk-Koezen JE, Timmerman H, Link R, Van der Goot H, IJzerman AP.
A novel class of adenosine A_3 receptor ligands. II. Structure affinity profile of a series of isoquinoline and quinazoline compounds.
J. Med. Chem. 41, 3994 - 4000 (1998)

Dalpiaz A, Townsend-Nicholson A, Beukers MW, Schofield PR, IJzerman AP.
Thermodynamics of full agonist, partial agonist and antagonist binding to wild type and mutant adenosine A_1 receptors.
Biochem. Pharmacol. 56, 1437 - 1445 (1998)

Pavan B, IJzerman AP.
In vitro pharmacokinetic and metabolic study of adenosine receptor agonists in rat and human whole blood.
Biochem. Pharmacol. 56, 1625 - 1632 (1998)

Schwartz T, IJzerman AP.
Principles of agonism: undressing efficacy.
TiPS 19, 433 - 436 (1998)

Van Tilburg EW, Van Muijlwijk-Koezen JE, IJzerman AP.
Medicinal chemistry of the human adenosine A_3 receptor.
Drug Dev. Res. 45, 182 - 189 (1998)

Rivkees S, IJzerman AP, Swanson T.
New insights into the molecular mechanisms of A_1 adenosine receptor action.
Drug Dev. Res. 45, 93 - 102 (1998)

Van der Graaf PH, Van Schaick EA, Visser SAG, IJzerman AP, Danhof M.
Mechanism-based pharmacokinetic-pharmacodynamic modelling of anti-lipolytic effects of adenosine A_1 receptor agonists in rats: prediction of tissue-dependent efficacy *in vivo*.
J. Pharmacol. Exp. Ther. 290, 702 - 709 (1999)

Van Tilburg EW, von Frijtag Drabbe Künzel JK, De Groote M, Vollinga RC, Lorenzen A, IJzerman AP.
N^6,5'-Disubstituted adenosine derivatives as partial agonists for the human adenosine A_3 receptor.
J. Med. Chem. 42, 1393 - 1400 (1999)

Rivkees S, Barbhaiya H, IJzerman AP.
Identification of the adenine binding site of the human A_1 adenosine receptor.
J. Biol. Chem. 274, 3617 - 3621 (1999)

PAGE 53/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Dalpiaz A, Scatturin A, Pavan B, Varani K, IJzerman AP, Borea PA.
Thermodynamic *in vitro* studies as a method to investigate the pharmacodynamic behavior of adenosine A_1 receptor ligands.
Pharmaceut. Res. 16, 1054 - 1058 (1999)

De Zwart M, Kourounakis A, Kooijman H, Spek AL, Link R, Von Frijtag Drabbe Künzel JK, IJzerman AP.
5'-N-Substituted carboxamidoadenosines as agonists for adenosine receptors.
J. Med. Chem. 42, 1384 - 1392 (1999)

Jacobson KA, IJzerman AP, Linden J.
1,3-Dialkylxanthine derivatives having high potency as antagonists at human A_{2B} adenosine receptors.
Drug Dev. Res. 47, 45 - 53 (1999)

Ingkanian K, Von Frijtag Drabbe Künzel JK, IJzerman AP, Verpoorte R.
The interference of linoleic acid fraction in some receptor binding assays.
J. Nat. Prod. 62, 912 - 914 (1999)

Ingkanian K, IJzerman AP, Taesotikul T, Verpoorte R.
Isolation of opioid active compounds from *Tabernaemontana pachysophon* leaves.
J. Pharm. Pharmacol. 51, 1441 - 1446 (1999)

Van der Klein PAM, Kourounakis AP, IJzerman AP.
Allosteric modulation of the adenosine A_1 receptor. Synthesis and biological evaluation of novel 2-amino-3-benzoylthiophenes as allosteric enhancers of agonist binding.
J. Med. Chem. 42, 3629 - 3635 (1999)

De Zwart M, Vollinga RC, De Groote M, Beukers MW, Sleegers DF, Von Frijtag Drabbe Kuenzel JK, IJzerman AP.
Potent antagonists for the human adenosine A_{2B} receptor. Derivatives of the triazolotriazine adenosine receptor antagonist ZM241385 with high affinity.
Drug Dev. Res. 48, 95 - 103 (1999)

Beukers MW, Kristiansen K, IJzerman AP, Edvardsen O.
TinyGRAP database: a bioinformatics tool to mine G protein-coupled receptor mutant data.
TIPS 20, 475 - 477 (1999)

Zuurmond HM, Hessling J, Blüml K, Lohse M, IJzerman AP.
Study of interaction between agonists and Asn293 in helix VI of human β_2-adrenergic receptor.
Mol. Pharmacol. 56, 909 - 916 (1999)

Horn F, Van der Wenden EM, Oliveira L, IJzerman AP, Vriend G.
Receptors coupling to G proteins: is there a signal behind the sequence?
Proteins 41, 448 - 459 (2000)

PAGE 54/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Garrido MJ, Gubbens-Stibbe JM, Tukker EJ, Cox EH, Von Frijtag Drabbe Künzel, IJzerman AP, Danhof M, Van der Graaf PH.
Pharmacokinetic-pharmacodynamic analysis of the EEG effect of alfentanil in rats following ß-funaltrexamine-induced μ opioid receptor "knockdown" *in vivo*.
Pharm. Res. 17, 653 - 659 (2000)

Ingkanian K, IJzerman AP, Verpoorte R.
Luteolin, an adenosine A_1 active compound from *Senna siamea*.
J. Nat. Prod. 63, 315 - 317 (2000)

Gao Z-G, IJzerman AP.
Allosteric modulation of A_{2A} adenosine receptors by amiloride analogues and sodium ions.
Biochem. Pharmacol. 60, 669-676 (2000)

Gao Z-G, Jiang Q, Jacobson KA, IJzerman AP.
Site-directed mutagenesis of human A_{2A} adenosine receptors. Involvement of Glu13 and His278 in ligand binding and sodium modulation.
Biochem. Pharmacol. 60, 661-668 (2000)

Vittori S, Lorenzen A, Stannek C, Costanzi S, Volpini R, IJzerman AP, Von Frijtag Drabbe Kuenzel JK, Cristalli G.
N-cycloalkyl derivatives of adenosine and 1-deazaadenosine as agonists and partial agonists of the adenosine A_1 receptor.
J. Med. Chem. 43, 250-260 (2000)

De Ligt RAF, Kourounakis AP, IJzerman AP.
Inverse agonism at G protein-coupled receptors: (Patho)physiological relevance and implications for drug discovery.
Br. J. Pharmacol. 130, 1-12 (2000)

De Zwart M, De Groote M, Van der Klein PAM, Van Dun S, Bronsing R, Von Frijtag Drabbe Kuenzel JK, IJzerman AP.
Phenyl-substituted N^6-phenyladenosines and N^6-phenyl-5'-N-ethylcarboxamidoadenosines with high affinity at human adenosine A_{2B} receptors.
Drug Dev. Res. 49, 85 - 93 (2000)

Wanner MJ, Von Frijtag Drabbe Künzel JK, IJzerman AP, Koomen GJ.
2-Nitro analogs of adenosine and 1-deazaadenosine: synthesis and selectivity in binding at the adenosine A_1, A_{2A} and A_3 receptor.
Bioorganic & Medicinal Chemistry Letters 10, 2141 - 2144 (2000)

Fierens FLP, Vanderheyden PML, Gaborik Z, Le Minh T, De Backer JP, Hunyady L, IJzerman AP, Vauquelin G.
Lys^{199} mutation of the human angiotensin type I receptor differentially affects the binding of surmountable and insurmountable non-peptide antagonists.
J Renin-Angiotensin-Aldosterone System 1, 283 - 288 (2000)

PAGE 55/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Beukers MW, den Dulk H, van Tilburg EW, Brouwer J, IJzerman AP. Why are A_{2B} receptors low-affinity adenosine receptors? Mutation of Asn273 to Tyr increases affinity of human A_{2B} receptor for 2-(1-hexynyl)adenosine.
Mol. Pharmacol. 58, 1349 - 1356 (2000)

Van Muijlwijk-Koezen JE, Timmerman H, Van der Goot H, Menge WMPB, Von Frijtag Drabbe Künzel JK, De Groote M, IJzerman AP. Isoquinoline and quinazoline urea analogues as antagonists for the human adenosine A_3 receptor.
J. Med. Chem. 43, 2227 - 2238 (2000)

Kourounakis AP, Van der Klein PAM, IJzerman AP. Elucidation of structure-activity relationships of 2-amino-3-benzoylthiophenes: study of adenosine A_1 allosteric enhancement versus antagonistic activity.
Drug Dev. Res. 49, 227 - 237 (2000)

Kourounakis AP, Visser C, De Groote M, IJzerman AP. Allosteric modulation of the rat adenosine A1 receptor: differential effects on agonist and antagonist binding.
Drug Dev. Res. 51, 207 - 215 (2000)

Kourounakis AP, Visser C, De Groote M, IJzerman AP. Differential effects of the allosteric enhancer PD81,723 on agonist and antagonist binding and function at the human wild type and a mutant (T277A) adenosine A1 receptor.
Biochem. Pharmacol. 61, 137 - 144 (2001)

Gao Z-G, Van Muijlwijk-Koezen JE, Chen A, Mueller CE, IJzerman AP, Jacobson KA. Allosteric modulation of A_3 adenosine receptors by a series of 3-(2-pyridinyl)isoquinoline derivatives.
Mol Pharm 60, 1057 - 1063 (2001)

IJzerman AP, Kourounakis AP, Van der Klein PAM. Allosteric modulation of G protein-coupled receptors.
Il Farmaco 56, 67 - 70 (2001)

Van Tilburg EW, Van der Klein PAM, De Groote M, Beukers MW, IJzerman AP. Substituted 4-phenyl-2-(phenylcarboxamido)-1,3-thiazole derivatives as antagonists for the adenosine A_1 receptor.
Bioorg Med Chem Lett 11, 2017 - 2019 (2001)

Van Muijlwijk-Koezen JE, Timmerman H, IJzerman AP. The adenosine A_3 receptor and its ligands.
Progress in Medicinal Chemistry (King FD and Oxford AW, eds), vol 38, Elsevier Science BV, 2001, pp. 61 - 113.

PAGE 56/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Van Muijlwijk-Koezen JE, Timmerman H, van der Sluis RP, van de Stolpe AC, Menge WMPB, Beukers MW, van der Graaf PH, de Groote M, IJzerman AP.
Synthesis and use of FSCPX, an irreversible adenosine A_1 antagonist, as a "receptor knock-down" tool.
Bioorg. Med. Chem. Lett. 11, 815 - 818 (2001).

Van Muijlwijk-Koezen JE, Timmerman H, Vollinga RC, Von Frijtag Drabbe Künzel JK, De Groote M, Visser S, IJzerman AP.
Thiazole and diathiazole analogues as novel class of adenosine receptor antagonists
J. Med. Chem. 44, 749 - 762 (2001)

Schrier SM, Van Tilburg E, Van der Meulen H, IJzerman AP, Mulder GJ, Nagelkerke JF.
Extracellular adenosine-induced apoptosis in mouse neuroblastoma cells: involvement of adenosine receptors and adenosine uptake.
Biochem. Pharmacol. 61, 417 - 425 (2001)

Van Tilburg EW, Van der Klein PAM, Von Frijtag Drabbe Kuenzel JK, De Groote M, Stannek C, Lorenzen A, IJzerman AP.
5'-O-Alkylethers of N^6,2-substituted adenosine derivatives: partial agonists for the adenosine A_1 and A_3 receptors.
J. Med. Chem. 44, 2966 - 2975 (2001)

Fredholm BB, IJzerman AP, Jacobson KA, Klotz K-N, Linden J.
International Union of Pharmacology. XXV. Nomenclature and classification of adenosine receptors.
Pharmacol. Rev. 53, 1 - 26 (2001)

Soudijn W, van Wijngaarden I, IJzerman AP
Allosteric modulation of G protein-coupled receptors.
Expert Opin. Ther. Patents 11, 1889 - 1904 (2001)

Van Tilburg EW, IJzerman AP.
C2,5'-disubstituted and N^6,C2,5'-trisubstituted adenosine derivatives and their different uses.
BP 0105337.0, issued March 3, 2001

Van Tilburg EW, IJzerman AP.
C2,C8-disubstituted adenosine derivatives, a process for their preparation and their different uses.
BP 0105335.4, issued March 3, 2001

De Ligt RAF, Kourounakis AP, Lorenzen A, Hill SJ, Visser C, Dissen M, IJzerman AP.
Sodium shifts as a means to classify adenosine A_1 receptor ligands.
Biochem. Pharmacol., submitted

PAGE 57/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Lorenzen A, Beukers MW, Van der Graaf PH, Lang H, Van Muijlwijk-Koezen J, De Groote M, Menge W, Schwabe U, IJzerman AP.
Modulation of agonist responses at the A_1 adenosine receptor by an irreversible antagonist, receptor-G protein uncoupling and by the G protein activation state.
Biochem. Pharmacol. 64, 1251-1265 (2002)

Den Haan JMM, Mutis T, Blokland E, IJzerman AP, Goulmy EAJM.
General T-cell receptor antagonists to immunomodulate HLA-A2-restricted minor histocompatibility antigen HA-1-specific T-cell responses.
Blood 99, 985-992 (2002)

Van Tilburg EW, Von Frijtag Drabbe Künzel JK, De Groote M, IJzerman AP.
Evaluation of C2,5'-disubstituted adenosine derivatives: selectivity and efficacy for the adenosine A_1, A_{2A} and A_3 receptor.
J. Med. Chem. 45, 420-429 (2002)

Schrier SM, Florea BI, Mulder GJ, Nagelkerke JF, IJzerman AP.
Apoptosis induced by extracellular ATP in the neuroblastoma cell line N1E-115: studies on involvement of P2 receptors and adenosine.
Biochem. Pharmacol. 63, 1119 - 1126 (2002)

Van Calenbergh S, Link A, Fujikawa S, De Ligt RAF, Vanheusden V, Golisade A, Blaton NM, Rozenski J, IJzerman AP, Herdewijn P.
5'-Deoxy congeners of 9-(3-amido-3-deoxy-□-D-xylofuranosyl)-N^6-cyclopentyladenine: new adenosine A_1 receptor antagonists and inverse agonists.
J. Med. Chem. 45, 1845 - 1852 (2002)

Gao Z-G, Kim SG, Soltysiak KA, Melman N, IJzerman AP, Jacobson KA.
Selective allosteric enhancement of agonist binding and function at human A_3 adenosine receptors by a series of imidazoquinoline derivatives.
Mol. Pharmacol. 62, 81 - 89 (2002)

Schrier SM, de Bont H, Mulder GJ, Nagelkerke JF, IJzerman AP.
Distinct mechanisms of apoptosis in N1E-115 mouse neuroblastoma cells induced by different concentrations of adenosine, (in preparation)

Schrier SM, Kuipers HF, Vreugdenhil E, Mulder GJ, IJzerman AP.
Protection by adenosine against cycloheximide-induced apoptosis in N1E-115 cells: involvement of the adenosine A_{2A} and A_3 receptor, (in preparation)

PAGE 58/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Del Carmine R, Ambrosio C, Sbraccia M, Cotecchia S, IJzerman AP, Costa T.
Mutations inducing divergent shifts of constitutive activity reveal different modes of binding among catecholamine analogues to the beta$_2$-adrenergic receptor.
Br. J. Pharmacol. 135, 1715 - 1722 (2002)

Soudijn W, van Wijngaarden I, IJzerman AP.
Allosteric modulation of G protein-coupled receptors.
Curr. Opin. Drug Disc. Dev. 5, 749-755 (2002)

Priego EM, Von Frijtag Drabbe Kuenzel J, IJzerman AP, Camarasa MJ, Perez-Perez MJ.
Pyrido[2,1-f]purine-2,4-dione derivatives as a novel class of highly potent human A_3 adenosine receptor antagonists.
J. Med. Chem. 45, 3337 - 3344 (2002).

Dalpiaz A, Pavan B, Ngo Ngos F, Franchetti P, IJzerman AP.
Temperature dependence of the affinity enhancement of selective adenosine A_1 receptor agonism: a thermodynamic analysis.
Eur. J. Pharmacol. 448, 123 - 131 (2002).

De Ligt AF, IJzerman AP.
Intrinsic activity at adenosine A_1 receptors: partial and inverse agonism.
Curr. Pharm. Des. 8, 2333 - 2344 (2002)

Gerlach M, Maul C, Jagusch U-P, Sundermann B, Fuhr M, IJzerman AP, Dissen-de Groote M.
Substituted pyrazolopyrimidines and thiazolopyrimidines.
WO 02/072585 A2 (19/9/2002)

Bueters TJH, Groen B, Danhof M, IJzerman AP, Van Helden HPM.
Therapeutic efficacy of the adenosine A_1 receptor agonist N^6-cyclopentyladenosine (CPA) against organophosphate intoxication.
Arch. Toxicol. 76, 650-656 (2002)

Bueters TJH, Van Helden HPM, Danhof M, IJzerman AP.
Effects of the adenosine A1 receptor allosteric modulators PD81,723 and LUF5484 on the striatal acetylcholine release.
Eur. J. Pharmacol. 454, 177-182 (2002)

Deghati PYF, Borghini A, van den Nieuwendijk AMCH, Dissen-de Groote M, IJzerman AP.
Inhibition of nucleoside transport by new analogs of nitrobenzylthioinosine.
Bioorg. Med. Chem. 11, 899-908 (2003)

Soudijn W, van Wijngaarden I, IJzerman AP.
Medicinal chemistry of adenosine A_1 receptor ligands.
Curr. Topics Med. Chem. 3, 355-367 (2003)

PAGE 59/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Soudijn W, van Wijngaarden I, IJzerman AP.
Stereoselectivity of drug-receptor interactions.
IDrugs 6, 43-56 (2003)

Soudijn W, van Wijngaarden I, IJzerman AP.
Enantioselectivity in Drug-Receptor interactions. In: Handbook of Experimental Pharmacology (Sterochemical aspects of drug action and disposition) vol. 153 (Eichelbaum, Testa, Somogyi, eds.), Springer Verlag, Berlin, 2003, pp. 161-182

Maul C, Sundermann B, Fuhr M, IJzerman AP, Dissen-de Groote M.
Verwendung von substituierten Pyrazolopyrimidinen als Liganden von Nucleosid-Transport-Proteinen und/oder von Purinorezeptoren.
DE 101 53 344 A1 (15/5/2003)

Gao Z-G, Melman N, Erdmann A, Kim SG, Mueller CE, IJzerman AP, Jacobson KA
Differential allosteric modulation by amiloride analogues of agonist and antagonist binding at A_1 and A_3 adenosine receptors.
Biochem. Pharmacol. 64, 525-534 (2003)

Bueters TJH, Joosen MJA, Van Helden HPM, IJzerman AP, Danhof M.
Adenosine A1 receptor agonist N6-cyclopentyladenosine affects the inactivation of acetylcholinesterase in blood and brain by sarin.
J. Pharmacol. Exp. Ther. 304, 1307-1313 (2003)

Bueters TJ, van Helden HP, IJzerman AP, Danhof M.
Low efficacy adenosine A_1 agonists inhibit striatal acetylcholine release in rats improving central selectivity of action.
Neurosci Lett. 343, 57-61 (2003)

Schaddelee MP, Voorwinden HL, van Tilburg EW, Pateman TJ, IJzerman AP, Danhof M, de Boer AG. Functional role of adenosine receptor subtypes in the regulation of blood-brain barrier permeability: possible implications for the design of synthetic adenosine derivatives.
Eur J Pharm Sci. 19, 13-22 (2003)

Van Tilburg EW, Gremmen M, von Frijtag Drabbe Kunzel J, de Groote M, IJzerman AP.
2,8-Disubstituted adenosine derivatives as partial agonists for the adenosine A_{2A} receptor.
Bioorg Med Chem. 11, 2183-2192 (2003)

Beukers MW, Wanner MJ, Von Frijtag Drabbe Kunzel JK, Klaasse EC, IJzerman AP, Koomen GJ.
N^6-cyclopentyl-2-(3-phenylaminocarbonyltriazene-1-yl)adenosine (TCPA), a very selective agonist with high affinity for the human adenosine A1 receptor.
J Med Chem. 46, 1492-1503 (2003)

PAGE 60/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Bueters TJ, IJzerman AP, van Helden HP, Danhof M.
Characterization of the pharmacokinetics, brain distribution, and therapeutic efficacy of the adenosine A_1 receptor partial agonist 2'-deoxy-N^6-cyclopentyladenosine in sarin-poisoned rats.
Toxicol Appl Pharmacol 192, 86-94 (2003)

Harrison PK, Bueters TJ, IJzerman AP, van Helden HP, Tattersall JE.
Partial adenosine A_1 receptor agonists inhibit sarin-induced epileptiform activity in the hippocampal slice.
Eur J Pharmacol 471, 97-104 (2003)

Bueters TJ, van Duivenvoorde LM, Danhof M, IJzerman AP, van Helden HP.
Cyclopentyladenosine and some of its low-efficacy derivatives inhibit striatal synaptosomal release of acetylcholine to a similar degree.
Eur J Pharmacol 481, 141-146 (2003)

Van Herk T, Brussee J, van den Nieuwendijk AM, van der Klein PA, IJzerman AP, Stannek C, Burmeister A, Lorenzen A.
Pyrazole derivatives as partial agonists for the nicotinic acid receptor.
J Med Chem 46, 3945-3951 (2003)

Cordeaux Y, IJzerman AP, Hill SJ
Coupling of the human A_1 adenosine receptor to different heterotrimeric G proteins; evidence for agonist-specific receptor conformations.
Br J Pharmacol, in press

Chang L, Brussee H, IJzerman AP
2,4,6-trisubstituted pyrimidines and their different uses
GB 0323137.0, issued October 3, 2003

Chang L, Brussee H, IJzerman AP
Pyrimidines substituted in the 2,4,6 positions and their different uses
GB 0323138.8, issued October 3, 2003

Beukers MW, van Oppenraaij J, van der Hoorn PPW, Blad CC, den Dulk H, Brouwer J, IJzerman AP
Random mutagenesis of the human adenosine A2B receptor followed by growth selection in yeast. Identification of constitutively active and gain of function mutations.
Mol Pharmacol, in press

Van den Nieuwendijk AMCH, Pietra D, Heitman L, Göblyös A, IJzerman AP.
Synthesis and biological evaluation of 2,3,5-substituted [1,2,4]-thiadiazoles as allosteric modulators of adenosine receptors.
J Med Chem, in press

PAGE 61/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Puetz C, Sundermann B, Sundermann C, IJzerman AP, Tromp R, von Frijtag Drabbe Kuenzel J.
New analogs of nitrobenzylthioinosine.
EP 1 352 910 A1, publication date October 15, 2003
WO 03/084975 A1, publication date October 16, 2003

PAGE 62/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Annex B

"isopentenyladenosine and cancer"

1: Ishii Y, Hori Y, Sakai S, Honma Y.
Control of differentiation and apoptosis of human myeloid leukemia cells by cytokinins and cytokinin nucleosides, plant redifferentiation-inducing hormones.
Cell Growth Differ. 2002 Jan;13(1):19-26.
PMID: 11801528 [PubMed - indexed for MEDLINE]

2: Meisel H, Gunther S, Martin D, Schlimme E.
Apoptosis induced by modified ribonucleosides in human cell culture systems.
FEBS Lett. 1998 Aug 21;433(3):265-8.
PMID: 9744808 [PubMed - indexed for MEDLINE]

3: Soma MR, Corsini A, Paoletti R.
Cholesterol and mevalonic acid modulation in cell metabolism and multiplication.
Toxicol Lett. 1992 Dec;64-65 Spec No:1-15. Review.
PMID: 1471162 [PubMed - indexed for MEDLINE]

4: Kersten H.
On the biological significance of modified nucleosides in tRNA.
Prog Nucleic Acid Res Mol Biol. 1984;31:59-114. Review.
No abstract available.
PMID: 6397775 [PubMed - indexed for MEDLINE]

5: Hacker B, Chang Y.
Increased cytotoxicity of N6-(delta 2-isopentenyl)adenosine in combination with pentostatin against L-1210 leukemia cells.
J Pharm Sci. 1983 Oct;72(10):1225-6.
PMID: 6606032 [PubMed - indexed for MEDLINE]

6: Hacker B, Chang Y.
Enhancement of the antitumor activity of N6-(delta 2-isopentenyl)adenosine against cultured L-1210 leukemia cells by pentostatin using a polymeric delivery system.
J Pharm Sci. 1983 Aug;72(8):902-5.
PMID: 6604803 [PubMed - indexed for MEDLINE]

7: Sonoki S, Ohno Y, Kijima N, Hishiyama T, Saito H, Sugiyama T, Hashizume T.
Relationship between adenylate cytokinin production and Ti plasmid of Agrobacterium tumefaciens.

PAGE 63/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Nucleic Acids Symp Ser. 1983;(12):111-4.
PMID: 6664842 [PubMed - indexed for MEDLINE]

8: Vold BS, Keith DE Jr, Slavik M.
Urine levels of N-[9-(beta-D-ribofuranosyl)purin-6-ylcarbamoyl]-L-threonine, N6-(delta 2-isopentenyl)adenosine, and 2'-O-methylguanosine as determined by radioimmunoassay for normal subjects and cancer patients.
Cancer Res. 1982 Dec;42(12):5265-9.
PMID: 7139629 [PubMed - indexed for MEDLINE]

9: Hargrove JL, Granner DK.
Inhibition of hepatoma cell growth by analogs of adenosine and cyclic AMP and the influence of enzymes in mammalian sera.
J Cell Physiol. 1982 Jun;111(3):232-8.
PMID: 6124549 [PubMed - indexed for MEDLINE]

10: Chang Y, Hacker B.
Antineoplastic effects of N6-(delta 2-isopentenyl)adenosine against L-1210 mouse lymphocytic leukemic cells using a polymeric delivery system.
J Pharm Sci. 1982 Mar;71(3):328-31.
PMID: 7069592 [PubMed - indexed for MEDLINE]

11: Huneeus VQ, Wiley MH, Siperstein MD.
Isopentenyl adenine as a mediator of mevalonate-regulated DNA replication.
Trans Assoc Am Physicians. 1980;93:347-56.
PMID: 7245580 [PubMed - indexed for MEDLINE]

12: Grindey GB, Lowe JK, Divekar AY, Hakala MT.
Potentiation by guanine nucleosides of the growth-inhibitory effects of adenosine analogs on L1210 and sarcoma 180 cells in culture.
Cancer Res. 1976 Feb;36(2 Pt 1):379-83.
PMID: 944090 [PubMed - indexed for MEDLINE]

13: Burns DM, Rodi CP, Agris PF.
Natural occurrence of an inhibitor of mammalian cell growth in human and mouse cells of normal and tumor origin.
Cancer Biochem Biophys. 1976;1(6):269-80.
PMID: 1035127 [PubMed - indexed for MEDLINE]

14: Rustum YM, Grindey GB, Hakala MT, Mihich E.
Multifactorial cellular determinants of the action of antimetabolites.
Adv Enzyme Regul. 1976;14:281-95. No abstract available.
PMID: 184698 [PubMed - indexed for MEDLINE]

PAGE 64/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

15: Mittelman A, Evans JT, Chheda GB.
Cytokinins as chemotherapeutic agents.
Ann N Y Acad Sci. 1975 Aug 8;255(751106-751230-2):225-34. No abstract available.

PMID: 1059358 [PubMed - indexed for MEDLINE]

16: Shavelson LJ, Tritsch GL.
Effect of N6-(delta2-isopentenyl)adenosine treatment in vivo on hexokinase
activity of mouse L 1210 cells.
J Med. 1975;6(2):181-8.
PMID: 1057642 [PubMed - indexed for MEDLINE]

17: Gallo RC, Whang-Peng J, Perry S.
Isopentenyladenosine stimulates and inhibits mitosis of human lymphocytes
treated with phytohemagglutinin.
Science. 1969 Jul 25;165(891):400-2. No abstract available.
PMID: 5789436 [PubMed - indexed for MEDLINE]

"mittelman a and adenosine"

1: Casper ES, Mittelman A, Kelsen D, Young CW.
Phase I clinical trial of fludarabine phosphate (F-ara-AMP).
Cancer Chemother Pharmacol. 1985;15(3):233-5.
PMID: 2414021 [PubMed - indexed for MEDLINE]

2: Dutta SP, Mittelman A, Chheda GB.
Metabolism of 1,N6-ethenoadenosine.
Biochem Med. 1980 Apr;23(2):179-84. No abstract available.
PMID: 7396887 [PubMed - indexed for MEDLINE]

3: Chheda GB, Hong CI, Gurwara SK, Mittelman A.
Metabolic fate of N6-benzyladenosine and N6-benzyladenosine-5'-phosphate in
rats.
J Pharm Sci. 1979 Aug;68(8):1054-6.
PMID: 480162 [PubMed - indexed for MEDLINE]

4: Catane R, Kaufman JH, Nime FA, Evans JT, Mittelman A.
Phase I study of N6-benzyladenosine-5'-monophosphate.
Cancer Treat Rep. 1978 Sep;62(9):1371-3. No abstract available.
PMID: 688280 [PubMed - indexed for MEDLINE]

5: Sufrin G, Tritsch GL, Mittelman A, Murphy GP.

PAGE 65/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

Adenosine deaminase activity in patients with carcinoma of the bladder.
J Urol. 1978 Mar;119(3):343-6.
PMID: 642089 [PubMed - indexed for MEDLINE]

6: Sufrin G, Tritsch GL, Mittelman A, Murphy GP.
Studies of lymphocyte adenosine deaminase activity in patients with renal and
transitional cell carcinoma.
Int Adv Surg Oncol. 1978;1:11-28. Review.
PMID: 399761 [PubMed - indexed for MEDLINE]

7: Sufrin G, Tritsch GL, Mittelman A, Moore RH, Murphy GP.
Adenosine deaminase activity in patients with renal adenocarcinoma.
Cancer. 1977 Aug;40(2):796-802.
PMID: 890659 [PubMed - indexed for MEDLINE]

8: Nechaev A, Halberg F, Mittelman A, Tritsch GL.
Circannual variation in human erythrocyte adenosine aminohydrolase.
Chronobiologia. 1977 Jul-Sep;4(3):191-8.
PMID: 598270 [PubMed - indexed for MEDLINE]

9: Tritsch GL, Nechaev A, Mittelman A.
Synergism between the antiproliferative activities of arabinosyladenine and
N6-benzyladenosine.
Cancer Biochem Biophys. 1977;2(2):87-90.
PMID: 567524 [PubMed - indexed for MEDLINE]

10: Tritsch GL, Niswander PR, Rosenfeld J, Nechaev A, Mittelman A.
Cosolvent-buffer mixtures as models for the cytoplasmic mileu: the enzymology
of adenosine aminohydrolase.
Mol Cell Biochem. 1976 Aug 30;12(2):93-101.
PMID: 986542 [PubMed - indexed for MEDLINE]

11: Keogh B, Pauly J, Tritsch G, Mittelman A, Murphy GP.
Adenosine-aminohydrolase activity in the erythrocytes, lymphocytes, and plasma
of healthy subjects and kidney transplant recipients.
J Surg Oncol. 1976;8(5):417-24.
PMID: 792572 [PubMed - indexed for MEDLINE]

12: Mittelman A, Evans JT, Chheda GB.
Cytokinins as chemotherapeutic agents.
Ann N Y Acad Sci. 1975 Aug 8;255(751106-751230-2):225-34. No abstract available.

PMID: 1059358 [PubMed - indexed for MEDLINE]

PAGE 66/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02

13: Hong CI, Tritsch GL, Mittelman A, Hebborn P, Chheda GB.
Synthesis and antitumor activity of 5'-phosphates and cyclic 3',5'-phosphates
derived from biologically active nucleosides.
J Med Chem. 1975 May;18(5):465-73.
PMID: 168381 [PubMed - indexed for MEDLINE]

14: Tritsch GL, Mittelman A.
Automated determination of adenosine aminohydrolase in human plasma and
erythrocytes by continuous flow analysis.
Biochem Med. 1975 Jan;12(1):66-71. No abstract available.
PMID: 1137571 [PubMed - indexed for MEDLINE]

15: Hong CI, Chheda GB, Murphy GP, Mittelman A.
Metabolism of N-(purin-6-ylcarbamoyl)-L-threonine riboside in rat and man.
Biochem Pharmacol. 1973 Aug 1;22(15):1927-36. No abstract available.
PMID: 4722460 [PubMed - indexed for MEDLINE]

16: Bhanalaph T, Mittelman A, Ambrus JL, Murphy GP.
Effects of chronic administration of adenosine on kidney and liver functions.
J Med. 1973;4(3):189-92. No abstract available.
PMID: 4520758 [PubMed - indexed for MEDLINE]

17: Bhanalaph T, Mittelman A, Ambrus JL, Murphy GP.
Effect of adenosine and some of its analogs on renal hemodyamics.
J Med. 1973;4(3):178-88. No abstract available.
PMID: 4149212 [PubMed - indexed for MEDLINE]

18: Chheda GB, Mittelman A.
N 6 -(2 -isopentenyl)adenosine metabolism in man.
Biochem Pharmacol. 1972 Jan;21(1):27-37. No abstract available.
PMID: 5066734 [PubMed - indexed for MEDLINE]

19: Tritsch GL, Mittelman A, Jones R Jr, Grace JT Jr.
N6-(Delta 2-isopentenyl) adenosine interference with methionine metabolism in
axemic cultures of mammalian cells.
Biochem Pharmacol. 1969 Jan;18(1):250-2. No abstract available.
PMID: 5780991 [PubMed - indexed for MEDLINE]

PAGE 67/80 * RCVD AT 11/22/2004 5:26:28 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:202 737 3528 * DURATION (mm-ss):21-02